

causing the displaceable moiety displaced from the first surface to contact a second surface bearing a capture moiety which specifically binds to the displaceable moiety, so as to capture the displaceable moiety on the second surface, said capture generating a detectable signal; and

detecting the signal; wherein said detection is performed by means other than Surface Plasmon Resonance, and wherein the [displaceable moiety cannot generate the] detectable signal [which is detected in the assay] is not generated unless and until the displaceable moiety is captured on the second surface whereupon said detectable signal indicating detection of analyte in said assay is generated.

Please amend claim 12 to read as follows:

12. (twice amended) A method according to claim 1, wherein the capture of the displaceable moiety by the capture moiety directly modulates [the] an electrochemical [properties] property of the capture moiety, which modulation comprises the detectable signal.

REMARKS

This amendment is filed to address issues raised in the parent case. Early consideration and allowance of the application are respectfully urged.

The Examiner states that claims 1-3, 5-16 and 20 are pending in this application, claim 22 presented in the amendment filed 4/30/01 having been renumbered as 20 by the Examiner. Applicants are confused as to the numbering of claims. In the initial PCT filing (of which this a national phase) there were 24 claims. In preliminary examination, these claims were amended, leaving 21 claims. The Examiner has made rejections referring to claim numbers which are consistent with these being the claims at issue. The Preliminary Amendment filed with the National Phase Application instructed the Patent Office to cancel claims 23 and 24, which had been in the parent case, but which had been renumbered as 20 and 21 during preliminary examination. It appears that this amendment was entered as cancelling claims 20 and 21 from the post-preliminary

examination claims. Thus, Applicants submits that the correct numbering of claims in this application should be 1-3, 5-16 and 22 and should use the post-preliminary examination set of claims as a starting point. To avoid ambiguity, the added claim is referred to in these remarks as "20/22".

In the parent application, the claims were rejected under 35 USC § 112, second paragraph. The Examiner identified two points which were alleged to give rise to ambiguity. Applicants have amended claim 1 in view of these remarks and additional observations of the newly appointed attorney to improve clarity. These amendments are believed to fully overcome the rejection under 35 USC § 112 based on a lack of antecedent basis in claim 1. Applicants have made a minor amendment to claim 12, to make it clear that it is only one electrochemical property which needs to be modulated. Beyond this modification, which is supported on Page 8, line 7 et seq of the application, Applicants respectfully traverse the rejection as applied to claim 12.

Claim 12 is a dependent claim which recites that the capture of the displaceable moiety by the capture moiety directly modulates the "electrochemical properties" of the displaceable moiety. The Examiner has asserted without explanation that the use of the term "electrochemical properties" renders the claims indefinite. Thus, the Examiner has made only a conclusory allegation and has not met the burden of establishing that a person skilled in the art would be unable to ascertain the scope of the claims (*Ex parte Cordova*, 10 U.S.P.Q. 2d 1949, 1952 (POBAI 1989)) ("it is incumbent on the Examiner to establish that one having ordinary skill in the art would not have been able to determine the scope of protection defined by the claim when read in light of the specification"). Furthermore, Applicants respectfully submit that there is nothing unclear or ambiguous about the term "electrochemical properties." Persons skilled in the art would understand the plain language of claim 12 to mean that the binding of the displaceable moiety results in a change in the properties of the capture moiety which can be measured using electrochemical techniques such as amperometry, voltametry or coulombetry (as opposed to detecting color for example). Such a change might be a change in the redox potential (the amount of potential difference necessary to cause an

oxidation or reduction reaction), or a change in the conductivity/resistance of the material or some similar change. Furthermore, this is precisely the definition which is provided in the specification on Page 8. Thus, Applicants submit that previous rejection under 35 USC § 112 has been fully overcome and should not be repeated. Should it be repeated, however, the Examiner is requested to explain why the language of claim 12 would be unclear to a person skilled in the art.

The Examiner also rejected claims 1-3, 7-10 and 13-16 under 35 USC § 102 as anticipated by Schram et al. Applicants respectfully submit that the amendments to claim 1 fully overcome this rejection. The Examiner in her remarks asserted that the language of the claims did not exclude the use of fluorescent or enzyme labels which can provide a detectable signal even when not bound. Applicants submit that this possible scope of the claims is plainly excluded by the amended language of claim 1. Thus, this rejection should not be repeated.

The Examiner also rejected claims 5-6, 11-12 and 20 as obvious over the combination of Schramm et al. and Tom-Moy et al. In making this rejection, the Examiner asserted that Schramm et al differed from these claims "by not specifically teaching detection by the generation or modulation of an acoustic wave." Since these claims are dependent on claim 1 which is discussed above, Applicants would point out that there is a further difference between the claims and Schramm, namely the nature of the detected signal. Furthermore, this combination of reference does not result in a method as in claim 12, because there is no detection in either reference via a change in an electrochemical property. Similarly, the Examiner has not alleged that either reference discloses the use of a fusion protein (claim 5) or a mimotope (claim 6) as the displaceable moiety, or the use of a mimotope as an intervening moiety (claim 20/22). Thus, at most this rejection would be of relevance to claim 11. Clarification of the basis for the rejection is requested if it is maintained.

The Examiner also rejected claims 1-16 and 20/22 as obvious over the combination of Garland et al. in view of Tom-Moy et al. The Examiner argued that Garland teaches a comparable assay using Surface Plasmon Resonance as a detection

means, and that modifying this technique to use a different detection system, such as the evanescent or acoustic wave technique of Tom-Moy would have been obvious. As stated in *Ex parte Hiyamizu*, 10 USPQ 2d 1393, 1394 (POBAI 1988), "citing references which merely indicate the isolated elements ... are known is not a sufficient basis for concluding that the combination of elements would have been obvious." What is required is something more, a suggestion or motivation in the art to make the asserted combination and an expectation of success. *In re Dow Chemical*, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988) ("The consistent criterion for determining obviousness is whether the prior art would have suggested...that this process should be carried out and would have a reasonable likelihood of success...Both the suggestion and the expectation must be found in art."). Applicants respectfully submit that the Examiner has failed to establish that this requirement is met in the present case.

The prior Examiner stated that one skilled in the art would have been motivated to substitute the detection system of Tom-Moy for that of Garland "in order to reduce steps and reagents by elimination [of] having to label the detectable moiety with a fluorescent, luminescence [sic] or radioactive tag." Applicants respectfully point out, however, that Garland does not employ any of these labeling techniques, so changes motivated by a desire to eliminate these techniques are irrelevant. Further, the technique of Tom-Moy does require a labeled moiety, namely the biotinylated antibody which is bound to an avidin-coated sensor.

The prior Examiner also asserted that the artisan would have an expectation of success because "Tom-Moy et al. teach that detecting modulation of acoustic waves reduces the user time required to customize the measurement surface." Applicants respectfully submit that this does not provide an expectation that a combined method would be successful. Indeed, this is an asserted characteristic of Tom-Moy's method for making the measuring device, and not of the method of using it in an assay.

Further, it should be noted that the mass biosensor of Tom-Moy apparently works in a liquid medium as depicted in Fig. 1 of Tom-Moy. The Examiner has not explained why the cited references provide any suggestion (without reliance on hindsight)

of utilizing this sensor in the context of a solid support such as that employed in Garland or Schramm. Thus, Applicants submit that the examiner has not presented a *prima facie* case of obviousness and that the rejection should therefore not be repeated.

For these reasons, and in view of the above amendments, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,



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